PCT/CU03/00004

NEW CLAIMS IN REPLY TO PCT WRITTEN OPINION

ANTIANGIOGENIC ACTIVE IMMUNOTHERAPY.

1. An immunogenic composition comprising VEGFR1 polypeptides and fragments thereof, or its encoding oligonucleotides, administered in the presence or not of a pharmaceutically accepted adjuvant.
2. A composition according to claim 1, wherein the antigen is of autologous, heterologous, or chimeric nature.
3. A composition according to claim 1, wherein the antigen is a mutant of the molecule.
4. A composition according to claim 1, wherein the immunogen is obtained from synthetic, recombinant, or natural sources.
5. A composition according to claims from 1 to 4 wherein the immunogen is administered as part of plasmidic or viral vectors.
6. A composition according to claim from 1 to 5, wherein the adjuvant is selected from the group consistent of: the recombinant particle of Hepatitis B Core Antigen, the recombinant particle of Hepatitis C Core Antigen, the OPC protein, the KLH protein, Freund adjuvant or its derivatives, and Montanide ISA 51
7. An immunogenic composition comprising VEGFR1 polypeptides and fragments thereof, or its encoding oligonucleotides, administered associated covalently or not to *Neisseria meningitidis* outer membrane derived VSSP preparations.
8. An immunogenic composition comprising VEGFR1 polypeptides and fragments thereof, or its encoding oligonucleotides, administered associated covalently or not to the p64K protein.
9. An immunogenic composition comprising VEGFR2 polypeptides and fragments thereof, or its encoding oligonucleotides, administered in the presence or not of a pharmaceutically accepted adjuvant.

10. A composition according to claim 9, wherein the antigen is of autologous, heterologous, or chimeric nature.
11. A composition according to claim 9, wherein the antigen is a mutant of the molecule.
12. A composition according to claim 9, wherein the immunogen is obtained from synthetic, recombinant, or natural sources.
13. A composition according to wherein the immunogen is administered as part of plasmidic or viral vectors.
14. A composition according to claims from 9 to 13, wherein the adjuvant is selected from the group consistent of: the recombinant particle of Hepatitis B Core Antigen, the recombinant particle of Hepatitis C Core Antigen, the OPC protein, the KLH protein, Freund adjuvant or its derivatives, and Montanide ISA 51
15. An immunogenic composition comprising VEGFR2 polypeptides and fragments thereof, or its encoding oligonucleotides, administered associated covalently or not to *Neisseria meningitidis* outer membrane derived VSSP preparations.
16. An immunogenic composition comprising VEGFR2 polypeptides and fragments thereof, or its encoding oligonucleotides, administered associated covalently or not to the p64K protein.
17. An immunogenic composition comprising VEGFR3, NRP-1 or NRP-2 polypeptides and fragments thereof, or their encoding oligonucleotides, administered in the presence or not of a pharmaceutically accepted adjuvant.
18. A composition according to claim 19, wherein the antigen is of autologous, heterologous, or chimeric nature.
19. A composition according to claim 19, wherein the antigens is a mutant of the molecule.
20. A composition according to claim 19, wherein the immunogen is obtained from synthetic, recombinant, or natural sources.
21. A composition according to wherein the immunogen is administered as part of plasmidic or viral vectors.
22. A composition according to claims from 17 to 21, wherein the adjuvant is selected from the group consistent of: the recombinant particle of Hepatitis B

Core Antigen, the recombinant particle of Hepatitis C Core Antigen, the OPC protein, the KLH protein, Freund adjuvant or its derivatives, and Montanide ISA 51.

23. An immunogenic composition comprising VEGFR3, NRP-1 or NRP-2 polypeptides and fragments thereof, or their encoding oligonucleotides, administered associated covalently or not to *Neisseria meningitidis* outer membrane derived VSSP preparations.
24. An immunogenic composition comprising VEGFR3, NRP-1 or NRP-2 polypeptides and fragments thereof, or their encoding oligonucleotides, administered associated covalently or not to the p64K protein.
25. An immunogenic composition comprising VEGF polypeptides and/or its encoding oligonucleotides, administered in the presence of an adjuvant.
26. An immunogenic composition comprising at least two of the preparations described in claims from 1 to 24
27. An immunogenic composition comprising VEGF and at least a molecule described in claims 1-3, 7-9 and 16-18, administered in the presence or not of a pharmaceutically accepted adjuvant.
28. An immunogenic composition comprising a bi-cistronic vector coding for a VEGFR1 or fragments thereof and a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP.
29. An immunogenic composition comprising a DNA vector coding for a VEGFR1 or fragments thereof and a DNA vector coding for a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP.
30. An immunogenic composition comprising a fusion protein containing a VEGFR1 or fragments thereof and a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP.
31. An immunogenic composition comprising VEGFR1 polipeptide or fragments thereof and a mutant of VEGF polipeptide administered in the presence of incorporated into *Neisseria meningitidis* outer membrane derived VSSP.

32. An immunogenic composition comprising a bi-cistronic vector coding for a VEGFR2 or fragments thereof and a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP.
33. An immunogenic composition comprising a DNA vector coding for a VEGFR2 or fragments thereof and a DNA vector coding for a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP.
34. An immunogenic composition comprising a fusion protein containing a VEGFR2 or fragments thereof and a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP.
35. An immunogenic composition comprising VEGFR2 polipeptide or fragments thereof and a mutant of VEGF polipeptide administered in the presence of incorporated into *Neisseria meningitidis* outer membrane derived VSSP.
36. Method for active vaccination characterized by the administration of an immunogenic composition comprising immunogenic VEGFR1 polypeptides and fragments thereof or its encoding oligonucleotides, administered in the presence or not of a pharmaceutically accepted adjuvant for the treatment of disorders associated to an increment of angiogenesis.
37. Method of claim 36 wherein the immunogen is of autologous, heterologous, or chimeric nature.
38. Method of claim 36 wherein the immunogen is a mutant of the molecule.
39. Method of claim 36 wherein the immunogen is obtained from synthetic, recombinant, or natural sources
40. Method of claim 36 wherein the immunogen is administered as part of plasmidic or viral vectors.
41. Method of claims wherein the adjuvant is selected from the group consistent of: the recombinant particle of Hepatitis B Core Antigen, the recombinant particle of Hepatitis C Core Antigen, the OPC protein, the KLH protein, Freund adjuvant or its derivatives, and Montanide ISA 51.

42. Method of claims wherein the immunogenic composition comprise VEGFR1 polypeptides and fragments thereof or its encoding oligonucleotides, administered associated covalently or not to *Neisseria meningitidis* outer membrane derived VSSP preparations, for the treatment of disorders associated to an increment of angiogenesis
43. Method of claims from 36 to 40 wherein the immunogenic composition comprise VEGFR1 polypeptides and fragments thereof or its encoding oligonucleotides, administered associated covalently or not to the p64K protein
44. Method for active vaccination characterized by the administration of an immunogenic composition comprising VEGFR2 polypeptides and fragments thereof or its encoding oligonucleotides, administered in the presence or not of a pharmaceutically accepted adjuvant for the treatment of disorders associated to an increment of angiogenesis.
45. Method of claim 44 wherein the immunogen is of autologous, heterologous, or chimeric nature.
46. Method of claim 44 wherein the immunogen is a mutant of the molecule.
47. Method of claim 44 wherein the immunogen is obtained from synthetic, recombinant, or natural sources
48. Method of claim 44 wherein the immunogen is administered as part of plasmidic or viral vectors.
49. Method of claims from 44 to 48 wherein the adjuvant is selected from the group consistent of: the recombinant particle of Hepatitis B Core Antigen, the recombinant particle of Hepatitis C Core Antigen, the OPC protein, the KLH protein, Freund adjuvant or its derivatives, and Montanide ISA 51
50. Method of claims from 44 to 48 wherein the immunogenic composition comprise VEGFR2 polypeptides and fragments thereof or its encoding oligonucleotides, administered associated covalently or not to *Neisseria meningitidis* outer membrane derived VSSP preparations, for the treatment of disorders associated to an increment of angiogenesis

51. Method of claims from 44 to 48 wherein the immunogenic composition comprise polypeptides or oligonucleotides coding for the VEGFR2 and fragments thereof, administered associated covalently or not to the p64K protein
52. Method for active vaccination characterized by the administration of an immunogenic composition comprising the VEGFR3, NRP-1 or NRP-2 polypeptides and fragments thereof, or its encoding oligonucleotides, administered in the presence or not of a pharmaceutically accepted adjuvant for the treatment of disorders associated to an increment of angiogenesis.
53. Method of claim 52 wherein the immunogen is of autologous, heterologous, or chimeric nature.
54. Method of claim 52 wherein the immunogen is a mutant of the molecule.
55. Method of claim 52 wherein the immunogen is obtained from synthetic, recombinant, or natural sources
56. Method of claim 52 wherein the immunogen is administered as part of plasmidic or viral vectors.
57. Method of claims from 52 to 56 wherein the adjuvant is selected from the group consistent of: the recombinant particle of Hepatitis B Core Antigen, the recombinant particle of Hepatitis C Core Antigen, the OPC protein, the KLH protein, Freund adjuvant or its derivatives, and Montanide ISA 51
58. Method of claims from 52 to 56 wherein the immunogenic composition comprise VEGFR3, NRP-1 or NRP-2 polypeptides and fragments thereof, or its encoding oligonucleotides, administered associated covalently or not to *Neisseria meningitidis* outer membrane derived VSSP preparations, for the treatment of disorders associated to an increment of angiogenesis
59. Method of claims from 52 to 56 wherein the immunogenic composition comprise VEGFR3, NRP-1 or NRP-2 polypeptides and fragments thereof, or its encoding oligonucleotides, administered associated covalently or not to the p64K protein
60. Method for active vaccination characterized by the administration of an immunogenic composition comprising VEGF polypeptides and fragments thereof, or its encoding oligonucleotides, administered in the presence or not of a pharmaceutically accepted adjuvant for the restoration or improvement of

immune functions, in immunologicaly compromised hosts, subjected or not to other disease-oriented vaccination procedures.

61. Method for active vaccination characterized by the administration of an immunogenic composition comprising at least two of the preparations described in claims from 1 to 24 for the treatment of disorders associated to an increment of angiogenesis
62. Method for active vaccination characterized by the administration of an immunogenic composition comprising VEGF and at least a molecule described in claims 1-3, 7-9 and 16-18, administered in the presence or not of a pharmaceutically accepted adjuvant for the treatment of disorders associated to an increment of angiogenesis
63. Method for active vaccination characterized by the administration of an immunogenic composition comprising a bi-cistronic vector coding for VEGFR2 or fragments thereof, and a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP preparations, for the treatment of disorders associated to an increment of angiogenesis.
64. Method for active vaccination characterized by the administration of an immunogenic composition comprising a DNA vector coding for VEGFR2 or fragments thereof and a DNA vector coding for a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP preparations for the treatment of disorders associated to an increment of angiogenesis.
65. Method for active vaccination characterized by the administration of an immunogenic composition comprising a fusion protein containing VEGFR2 or fragments thereof and a mutant of VEGF administered in the presence of or incorporated into the *Neisseria meningitidis* outer membrane derived VSSP preparation, for the treatment of disorders associated to an increment of angiogenesis.
66. Method for active vaccination characterized by the administration of an immunogenic protein composition comprising VEGFR2 or fragments thereof, and

a mutant of VEGF, administered in the presence of incorporated into *Neisseria meningitidis* outer membrane derived VSSP preparations, for the treatment of disorders associated to an increment of angiogenesis.

67. Method for active vaccination characterized by the administration of an immunogenic composition comprising a bi-cistronic vector coding for VEGFR1 or fragments thereof, and a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP preparations, for the treatment of disorders associated to an increment of angiogenesis.
68. Method for active vaccination characterized by the administration of an immunogenic composition comprising a DNA vector coding for VEGFR1 or fragments thereof and a DNA vector coding for a mutant of VEGF, administered in the presence of or incorporated into *Neisseria meningitidis* outer membrane derived VSSP preparations for the treatment of disorders associated to an increment of angiogenesis.
69. Method for active vaccination characterized by the administration of an immunogenic composition comprising a fusion protein containing VEGFR1 or fragments thereof and a mutant of VEGF administered in the presence of or incorporated into the *Neisseria meningitidis* outer membrane derived VSSP preparation, for the treatment of disorders associated to an increment of angiogenesis.
70. Method for active vaccination characterized by the administration of an immunogenic protein composition comprising VEGFR1 or fragments thereof, and a mutant of VEGF, administered in the presence of incorporated into *Neisseria meningitidis* outer membrane derived VSSP preparations, for the treatment of disorders associated to an increment of angiogenesis.
71. Method according to claims from 36 to 59 and from 61 to 70, for the treatment of tumors in mammals.
72. Method according to claims from 36 to 59 and from 61 to 70, for the treatment and prevention of tumors in humans.

73. Method according to claims from 36 to 59 and from 61 to 70, for the treatment of diseases characterized by an increment in the angiogenesis, as in malignant neoplasia and their metastasis in humans.
74. Method according to claims from 36 to 59 and from 61 to 70, for the treatment of entities characterized by an increase in the angiogenesis, as occurs in benign neoclassical.
75. Method according to claims from 36 to 59 and from 61 to 70, for the treatment of diseases characterized by an increment in the angiogenesis, as occurs in acute and chronic inflammatory processes.
76. Method according to claims from 36 to 59 and from 61 to 70, for the treatment of diseases characterized by an increment in the angiogenesis, as occurs in autoimmune processes.
77. Method according to claims from 36 to 59 and from 61 to 70, for the treatment of diseases characterized by an increment in the angiogenesis, as occurs in ocular alterations.
78. Method according to claims 60 and from 67 to 70, for the restoration or improvement of immune function, in immunologicaly compromised hosts, subjected or not to other disease-oriented vaccination procedures.
79. Method according to claims from 36 to 59 and from 61 to 70, for the treatment of diseases characterized by an increment in the angiogenesis, specifically in affective animals and cattle.